Original Research Article

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Cartilage erosion in laryngeal and hypopharyngeal cancer correlation between radiology and histopathology

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ABSTRACT

Background: The aim of this study was to assess the accuracy of preoperative contrast enhanced computed tomography (CECT) of neck with or without magnetic resonance imaging (MRI) in determining cartilage erosion in patients with laryngeal and hypo pharyngeal cancers and correlate this with the final histopathology report (HPE).

Methods: Forty patients diagnosed clinically with stage 3 laryngeal and hypo pharyngeal cancer were subjected to flexible laryngoscopy and CECT of neck. Patients with doubtful cartilage erosion on CECT were subjected to additional MRI. Radiologic findings including cartilage sclerosis, invasion and penetration on CECT and MRI were then correlated with HPE in patients who underwent total laryngectomy.

Results: CECT scan showed cartilage invasion in 30 cases. There were ten patients with doubtful cartilage erosion on the CECT scan who were then subjected to additional limited MRI which was compared with CECT scan and operative findings. Thyroid cartilage erosion was confirmed on MRI in five of the ten cases where CECT scan findings were equivocal. CECT scan failed to predict cricoid and arytenoid cartilage invasion in five cases and six cases respectively. Though MRI was a problem-solving tool, it had one false positive result.

Conclusions: CECT scan helped to identify cartilage erosion in 91.3% of cases which immensely contributed to the staging and treatment planning of laryngeal and hypo pharyngeal cancers. When findings on CECT are equivocal, the addition of MRI improves the accuracy of detecting cartilage involvement.

Keywords: Cartilage erosion, Contrast enhanced computed tomography, Magnetic resonance imaging, Laryngeal and hypopharyngeal cancer

INTRODUCTION

Laryngeal malignancy is the second common malignancy of the upper aero digestive tract, the first being malignancies arising from the oral cavity. 90% of these malignancies arise from the epithelial lining of the larynx and hence are histologically squamous cell tumors. These carcinomas commonly affect the glottis. They can also develop from various premalignant lesions of the larynx. Early detection and treatment of laryngeal cancer is of paramount importance.

The standard of care for patients diagnosed with advanced laryngeal cancers was changed after the publication of Veterans administration laryngeal trial in 1991. Radiation trial oncology group 91-11(RTOG 91-11) was another important trial 2 which demonstrated that concurrent chemo radiation had higher laryngeal preservation rates when compared to induction chemotherapy alone. One of the limitations of this trial was that it excluded patients with large volume T4 disease.²

According to American joint committee on cancer staging system (AJCC) until the 6th edition, stage T4a was defined as "tumour invades through the thyroid cartilage/tissue beyond the larynx". Minor cartilage erosion was staged as T3 disease. With the advent of improvement in technology, we can differentiate inner cortical thyroid cartilage erosion from penetration of thyroid cartilage cortex. The seventh edition of AJCC improved the precision of staging systems by differentiating the inner thyroid cartilage erosion (T3) from erosion of outer thyroid cartilage cortex.

For research on laryngeal cartilage invasion, European authors have extensively reviewed the CT, MR imaging and pathologic findings associated with cartilage invasion. The thyroid cartilage may be either chondrified or ossified, it is the most difficult cartilage of the larynx to evaluate for tumour erosion. Becker et al looked at various CT findings which includes sclerosis, erosion and lysis of cartilage in evaluating the thyroid, cricoid and arytenoid cartilage. Becker et al found that erosion or lysis of cartilage yielded the higher, approximately 83% specificity with a sensitivity of 71%, particularly for assessing thyroid cartilage involvement. But in contrast, authors found that accuracy rate of cricoid and arytenoid cartilage erosion is much higher when compared to thyroid cartilage.

On MRI, either high signal intensity within the cartilage on fat suppressed T2 eighted scans or cartilage enhancement on post contrast T1 Weighted images appear to be the more accurate criteria for diagnosing cartilage involvement. Various studies done by Becker et al, Zbaren et al and Castelijns et al showed that MR imaging is more sensitive (89%) than CT (64%) scan to detect the cartilage erosion. But the specificity for MRI is only 79% when compared to CT (92%). Overall accuracy of MRI is more than CT by 2% to 10%.

According to 2009 consensus statement on Larynx Preservation Clinical Trial Design, it was suggested that, in patients with T4 disease when the tumour extends through the cartilage into soft tissue of the neck should undergo laryngectomy. In these patients, laryngeal preservation is contraindicated.

In clinical practice, we need to depend on imaging to decide on the T4 disease. In our study we aimed at determining the accuracy of cartilage invasion by comparing the CT and MR imaging with final histopathological results.

METHODS

Institutional review board and ethical clearance was obtained for the conduct of this prospective study. Consecutive patients diagnosed to have stage 3 laryngeal cancer, based on clinical and endoscopic evaluation, between April 2014 to December 2016 at Christian Medical College, Vellore were recruited. Patients who

experienced treatment failure with prior radiation therapy and underwent salvage laryngectomy were also included from this study.

A sample of 40 patients was required to obtain a 95% confidence interval of $\pm 10\%$ around a positive predictive value of 88% in CT scan.

n= 4pq/d², p=positive predictive value=88%, d=10%

All clinically diagnosed patients with stage 3 laryngeal cancers were subjected to contrast enhanced CT scan (from skull base to mediastinum) as a standard protocol of initial evaluation and staging. Patients with equivocal cartilage erosion on CT were subjected to additional limited axial MRI (high resolution short Tau inversion recovery (STIR) and T2W axial sequences) of the larynx.

Patients with the biopsy proven laryngeal malignancies (T3 and T4 with cartilage erosion and/or extra laryngeal spread) were advised to undergo a total laryngectomy, partial pharyngectomy and the surgical laryngectomy specimen was sent for histopathological examination.

A section of the anterior commissure was also always submitted for histopathological assessment. Longitudinal sections were taken that included the false cord, ventricle, and true cord. Thyroid and cricoids cartilage were examined grossly and sampled adjacent to tumour, to document the presence or absence of cartilage invasion. In cases where the cartilages were ossified, the sections were decalcified before further processing.

Based on the CT imaging appearances, we categorized the state of the thyroid cartilage into four possible conditions; normal, sclerosis, invasion, penetration. In our categorization of the thyroid cartilage, Invasion was defined as destruction of the inner cortex of the thyroid cartilage but preservation of the outer cortex. Patients who had tumour through both the inner and outer thyroid cartilage were classified as having penetration. For our radiologic classification of the thyroid cartilage, the conditions of Invasion and Penetration were mutually exclusive. For the arytenoids and the cricoid cartilage, the categories of Invasion and Penetration were combined into a single destruction category.

RESULTS

Of the forty-studied population, thyroid cartilage invasion was present in twenty-three cases on CT scan, but seen in thirty-two cases in histopathology. Therefore CT scan failed to diagnose thyroid cartilage invasion in nine cases. Cricoid cartilage invasion was present in four cases on CT scan, but seen in eleven cases on histopathology. CT scan failed to diagnose cricoid cartilage invasion in seven cases. Arytenoid cartilage invasion was present in two cases on CT scan, but seen in nine cases on histopathology. CT scan again failed to diagnose arytenoid cartilage invasion in seven cases. In ten cases in

which there was doubtful cartilage invasion on CT scan, additional MRI was done. Thyroid cartilage invasion was present in five of these 10 cases both on MRI scan and histopathology. Seven cases had cricoid cartilage

invasion on both MRI scan and histopathology. Eight case had arytenoid cartilage invasion on MRI but seven cases on histopathology. MRI had one false positive result.

Table 1: Pathologically observed thyroid cartilage infiltration versus CT signs.

Thyroid cartilage: CT signs							
Pathology	Normal	Sclerosis	Invasion	Penetration	Total		
Normal	2	4	0	2	8		
Invasion	3	0	1	2	6		
Penetration	3	5	1	17	26		
Total	8	9	2	21	40		
Cricoid cartilage: CT signs							
	Normal	Sclerosis	Destruction	Total			
Normal	15	6	8	29			
Invasion	1	1	1	3			
Penetration	1	4	3	8			
Total	17	11	12	40			
Arytenoid cartilage: CT signs							
	Normal	Sclerosis	Destruction	Total			
Normal	15	12	4	31			
Invasion	2	3	0	5			
Penetration	1	1	2	4			
Total	18	16	6	40			

Abbreviation: CT, computed tomography.

Table 2: Pathologically observed thyroid cartilage findings versus MRI.

Thyroid cartilage: histopathology							
MRI additional	Normal	Invasion	Penetration	Total			
Normal	1	0	2	3			
Sclerosis	2	0	0	2			
Destruction	0	1	4	5			
Total	3	1	6	10			
Cricoid cartilage: histopathology							
MRI	Normal	Invasion	Destruction	Total			
Normal	1	0	2	3			
Invasion	3	2	0	5			
Destruction	1	0	1	2			
Total	5	2	3	10			
Arytenoid cartilage: histopathology							
MRI	Normal	Sclerosis	Destruction	Total			
Normal	1	0	2	3			
Invasion	3	2	0	5			
Penetration	1	0	1	2			
Total	5	2	3	10			

Abbreviation: MRI, magnetic resonance imaging HPE, histopathology.

DISCUSSION

The accurate evaluation of cartilage erosion is needed for the appropriate treatment strategies for laryngeal and hypopharyngeal cancers. Those cancers without cartilage erosion are treated with laryngeal organ preservation protocols. Partial laryngeal surgeries or chemoradiation have also been recently introduced for cases with limited cartilage invasion. Advanced staged disease with cartilage erosion and extra laryngeal spread needs to be treated with total laryngectomy.¹⁰

CECT is a good imaging modality for staging laryngeal and hypopharyngeal cancers, for determining the cartilage invasion, but, nevertheless, presents challenges. The CT appearances of laryngeal cartilage vary according to different proportions of hyaline cartilage, cortical bone and fatty marrow. Moreover, the nonossified cartilage and tumour show similar CT value of around 100 HU making them almost indistinguishable, especially when the tumour extends very near to the non-ossified cartilage.



Figure 1: 3 Tesla MRI limited STIR HR axial section showed thyroid cartilage invasion.

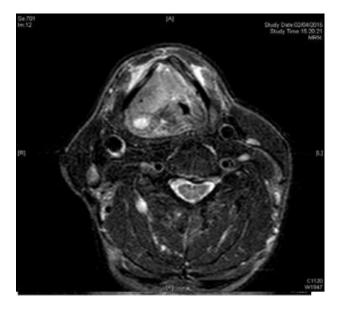


Figure 2: MR limited section showed arytenoid cartilage invasion.

Various studies have been done to assess the accuracy of CT scan which includes studies on single section CT and multi-section CT. Multi-slice CT has made progress in image interpretation, but, cartilage invasion is still over estimated, resulting in unnecessary total laryngectomies. Currently dual energy CT is under investigation for assessing cartilage invasion.

MRI has a similar ability as CT to define the interface between fat and tumour. But MRI is superior to assess the cartilage invasion. However, CT evaluation is much faster than MRI, substantially reducing or eliminating artefacts induced by movements attributable to breathing, swallowing, or coughing.¹¹

In our study thirty-nine (97%) patients were male and one (3%) was female. 38 of these underwent laryngectomy. Remaining two patients underwent Radiotherapy (One of these patients did not show cartilage invasion on CT or MRI and hence subjected to organ preserving radiotherapy while another patient had unresectable disease in view of prevertebral muscle involvement). Of the thirty-eight patients, thirty-two underwent primary upfront laryngectomy and the remaining six cases were salvage laryngectomies for post RT recurrences. Six patients who had salvage laryngectomies had initially refused surgery despite CT showing evidence of cartilage erosion.

The age of patients ranged between the third decades to the eight decades with a mean of 74 years. Of the total of 40 patients, 8% were less than 40 years of age, the majority (84%) were between 40 to 70 years, and 8% were more than 70 years of age. Nineteen patients had glottic carcinoma, ten patients had carcinoma hypopharynx, eleven patients had supraglottic carcinoma and two had transglottic carcinoma.

In our study of forty patients, computed tomography revealed thyroid cartilage involvement in twenty-three cases, however, thirty-two cases had thyroid cartilage invasion on histopathology. Thus, CT showed a false negative in 9 cases. Similarly cricoid cartilage involvement was seen in only 4 cases on CT scan in contrast to 11 cases on histology. Histopathological analysis picked up 9 cases of arytenoid cartilage involvement whereas CT scan revealed only 2 cases of arytenoid involvement. Thus, CT failed to pick up 7 cases of cricoid involvement and arytenoid cartilage involvement each.

Ten patients in whom CT scan showed suspicious cartilage erosion, but, was not conclusive, additional limited STIR and T2W axial images through the larynx were obtained. Thyroid cartilage invasion was confirmed on MRI in 5 patients which was later proven on histopathology. MRI was also able to diagnose cricoid cartilage invasion in all 7 patients. However, MRI showed arytenoid cartilage involvement in 8 cases although histopathology confirmed in only seven cases. Hence MRI had a false positivity in detecting arytenoid cartilage involvement.

A meta-analysis of the major studies showed that the accuracy of MR imaging is better than CT scanning on a McNemar test with a p value of 0.06. Many authors therefore recommend MR imaging as the primary

modality in evaluating cartilage involvement in patients with laryngeal carcinomas.

In our study, we utilised a 3 Tesla MRI STIR sequence axial cuts to assess the larynx, MRI had a higher sensitivity in predicting thyroid cartilage erosion. In contrast to the above mentioned studies we looked at the sensitivity and specificity of MRI in each of the 3 subsites i.e. thyroid cartilage, cricoid cartilage and arytenoid cartilage. MRI had 100% sensitivity in detecting thyroid cartilage invasion.

CONCLUSION

Contrast enhanced computed tomography scan helped in the identification of thyroid cartilage invasion accurately in 91.3% of cases and this immensely contributed to the staging and treatment planning of stage 3 and stage 4 laryngeal cancers. The addition of limited MRI through the larynx in patients with doubtful CT findings, improved the accuracy of the diagnosis of cartilage erosion. By restricting the use of MRI to patients with equivocal CT findings and confining to limited sequences and field of view, both the costs involved and time factors are kept to a minimum.

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